\_\_\_\_\_\_

Sequence Listing was accepted.

If you need help call the Patent Electronic Business Center at (866) 217-9197 (toll free).

Reviewer: Anne Corrigan

Timestamp: Mon Aug 13 14:44:44 EDT 2007

\_\_\_\_\_

## Validated By CRFValidator v 1.0.2

Application No: Version No: 10552571 1.1

Input Set:

Output Set:

**Started:** 2007-08-13 14:43:46.045 Finished:

2007-08-13 14:43:47.352

Elapsed: 0 hr(s) 0 min(s) 1 sec(s) 307 ms

Total Warnings:

Total Errors: 0

No. of SeqIDs Defined: 26

> Actual SeqID Count: 26

## SEQUENCE LISTING

<110> Barton, Barry Jensen, Susan Griffin, Alison Michelle Wong, Annie <120> Process for improving the manufacture of clavams e.g. clavulanic acid <130> PB60213 10/552,571 < 140> <141> 2005-10-11 <150> PCT/EP04/04001 <151> 2004-04-13 <150> GB030896.4 <151> 2003-04-15 <160> 26 <210> 1 <211> 1314 <212> DNA <213> Streptomyces clavuligerus <400> 1 60 atgttccacc cggtcctgcc ccggggccgc gaggaccgca ccgttctggt ctccggccgc ggctgcaccg tacgggacac cgaagggcgc acctatctcg acgcctcgtc ggtgctcgga 120 180 ctgacccaga tcggccatgg acgtgaggag atcgcgcagg ccgccgccga gcagatgcgg 240 acacteggte acttecacae etggggeace ateageaacg acaaggeeat eegactggee gegegeetea eegaeetgge geeeeagggt etceagegeg tetaetteae eageggegge 300 ggcgagggcg tcgagatcgc cctgcgcatg gcccgttact tccaccaccg caccggcagc 360 ccggagcgca cctggatctt gtcgcgccgc accgcctacc acggcatcgg ctacggcagc 420 480 ggtacggtgt cgggctcgcc cgcctaccag gacgggttcg gcccggtgct gccccatgtg caccacctca cgccgcccga cccgtaccac gccgagctgt acgacggcga ggacgtcacg 540 gagtactgcc tgcgcgaact cgcccgcacc atcgacgaga tcggccccgg gcggatcgcc 600 gcgatgatcg gggagccggt catgggcgcg ggcggcgccg tcgtcccgcc gccggactac 660 tggccgcgcg tcgccgcgct gctgcgctcc cacggcatcc tgctgatcct ggacgaggtc 720 780 gtcaccgcgt tcggccgcac ggggacctgg ttcgcggccg agcacttcgg ggtgaccccc gatetgetgg tgacegegaa gggeateace teegggtatg teeegeaegg ggeggtgete 840 ctgaccgagg aggtcgcgga cgccgtgaac ggggagacgg ggttcccgat cggcttcacc 900 tataccggtc accccacggc gtgcgccgtc gcgctcgcca atctcgacat catcgaacgg 960 gaagggctgc tggagaacgc ggtgaaggtg ggcgaccacc tcgccgggcg gctggcggcc 1020 ctgcgcgggc tgcccgccgt gggggacgtc cggcaactgg gcatgatgct cgccgtcgag 1080 1140 ctggtgtcgg acaagacggc ccgcaccccg ctgccgggcg gcaccctcgg ggtcgtggac 1200 gcgctgcgcg aggacgcggg cgtcatcgtc cgggccacgc cgcgctccct ggtcctcaat 1260 ccggcgctcg tgatggaccg ggccacggcg gacgaggtgg cggacgggct ggactcggtg ctgcggcggc tggcacccga cgggcggatc ggcgcggccc cccggcgggg gtga 1314 <210> 2 <211> 2464

<212> DNA

<213> Streptomyces clavuligerus

<400> 2

```
60
gtgtacgagt gcagcgatga ggttcgtcac gacgtccccg gcctgccggg tccgtcaccg
                                                                       120
tecateaceg teetgggetg tetgggegta egegeegaeg geeggaaaet ggagetggge
                                                                       180
cctccgcgtc agegggccgt tttcgccctg ctgctcatca acgcgggcag tgtggtgccg
gtcgactcga tcgtcttccg tatctggggc aactcaccac cgggcgcggt caccgcgacg
                                                                       240
                                                                       300
etccagtect atgtgteecg getgeggaaa etcetggeeg agtgtgtget eeeggaeggt
                                                                       360
tegacaceeg aactgetgea eeageegeeg ggetacacee tegegetegg caeegageae
                                                                       420
atcgacgcga accgttttga gcaggccatc aggacagggc gccggctctc gcgcgaggag
                                                                       480
cagcaccagg aggcgcgggc cgtgctctgc caggccctgc tgagctgggg cgggacaccg
tacgaggage tgagegegta egaettegee gtecaggagg ecaategget ggageagete
                                                                       540
                                                                       600
cggctgggcg ccgtggagac atgggcgcac tgctgtctgc ggctggggcg ggacgaggag
                                                                       660
gtgatggacc agctcaagcc ggaggtgcag cgcaatccgc tgcgggagcg gctgatcggg
cageteatge aggegeagta ceggetgggg tgecaggegg aegegeteag gaegtaegag
                                                                       720
                                                                       780
gcgacgcggc gggccctggc cgaggagctg gggaccgatc cgggcaagga gctggcggcg
ctgcacgcgg cgatcctgcg tcaggacaac ggtctggacc gcgtcgtccc ggcgtccgcg
                                                                       840
                                                                       900
ccgccgtcgg cgggggtcgg gcggggggcc gtgacggtgt cggtcccggc acagcggtcg
                                                                       960
aggccgttga cgcggccggt ggcggggcgg gcgcgggtcc cgggggcgat gacggtggcg
gegggegegg gggeggeece egegteegee teeggeteeg ttteegegte egttteegge
                                                                      1020
                                                                      1080
teeggeteeg geteeggete egeteetgeg teggtteeea eettetttee eggeteegtt
                                                                      1140
tetggetegg egteegttge egegteegta geegegeeeg titeeggeea tgteteeggg
eccgggteeg etttegggte egtggegete caeeggeege agaeeeteeg gggegageeg
                                                                      1200
                                                                      1260
gtccacgggg gcgcgcaggg gatgcgcacc gggcaggtgt tccccacgct gccgccgttc
                                                                      1320
gtegggegeg gegaegaget gegeggtetg etggagteeg egaegteege gttecaeaee
                                                                      1380
teggggeggg tggegttegt egteggegag gegggeageg geaagaeeeg geteetetee
                                                                      1440
gagttggage geteggttee ggaeagtgtg egeacegtet gggegteetg tteggagagt
gaggaccggc ccgactactg gccgtggacg accgtgctgc ggcatctgta cgcgatgtgg
                                                                      1500
                                                                      1560
ccggaacgta tgcacggatt ccccggttgg ctgcggcgcg cactcgcgga actgcttccc
gaggtgggee eggageeaca ggggeegeae teeeeegaeg ggggegagga gaacagegge
                                                                      1620
                                                                      1680
aacggggacg gtgcgggcga cggggacagc accccggcgc acaccctcac gctcgcgccc
                                                                      1740
gctctcgcgc ccccgcgctc cagagaggct cgtttcaccc tgcacgacgc cgtgtgccag
gcgcttctgc gcacggtccg cgaacccgtg gtgatcatgc tggaggacat ggagcgggcc
                                                                      1800
                                                                      1860
gacgccccct cgctcgccct gctgcgcctc ctggtggagc aactgcgcac cgtccccctg
                                                                      1920
ctgctcgtgg tcaccacgcg caccttccgg ctcgcgcacg acgccgagct gcgacgggcc
                                                                      1980
geegeegtga teeteeagte gaeeggegeg egeegggtee tgetgaaege eetggaegea
egggeeaeeg gggaaetege eggagggatg etgggeaagg eeeeggaeae eeteetegta
                                                                      2040
egggeeetge acgagegete egeegggaac eegtaettee tegteeaget eeteegeteg
                                                                      2100
                                                                      2160
ctccggcagg ggctcgccgc cgcctgggag acggagatcc cggacgagct ggccggggtc
                                                                      2220
gtgctgcaac ggctgtcgag cgtgccgccc gccgtgcgcc gggtgctcga catctgcgcg
                                                                      2280
gtcgtggagc gcagttgcga acggcgtgtg atcgagaccg tgctgcgcca tgagggaatc
ccgctggaga acgtccgtac ggcggtccgc ggcggtctgc tggaggaaga ccccgacgac
                                                                      2340
eccgggegge tgaggttegt geateegetg gteegggagg eegtetggga egaeetggag
                                                                      2400
aacacccgtc ggcccgtstc vmargtcccg ttcctccgcg ctcggggcgc tggccacggt
                                                                      2460
                                                                      2464
ctga
```

<210> 3 <211> 437 <212> PRT <213> Streptomyces clavuligerus

<400> 3

Glu Glu Ile Ala Gln Ala Ala Glu Gln Met Arg Thr Leu Gly His 55 Phe His Thr Trp Gly Thr Ile Ser Asn Asp Lys Ala Ile Arg Leu Ala 70 75 Ala Arg Leu Thr Asp Leu Ala Pro Gln Gly Leu Gln Arg Val Tyr Phe 85 90 Thr Ser Gly Gly Glu Gly Val Glu Ile Ala Leu Arg Met Ala Arg 105 110 100 Tyr Phe His His Arg Thr Gly Ser Pro Glu Arg Thr Trp Ile Leu Ser 115 120 Arg Arg Thr Ala Tyr His Gly Ile Gly Tyr Gly Ser Gly Thr Val Ser 135 140 Gly Ser Pro Ala Tyr Gln Asp Gly Phe Gly Pro Val Leu Pro His Val 155 150 His His Leu Thr Pro Pro Asp Pro Tyr His Ala Glu Leu Tyr Asp Gly 165 170 Glu Asp Val Thr Glu Tyr Cys Leu Arg Glu Leu Ala Arg Thr Ile Asp 185 180 Glu Ile Gly Pro Gly Arg Ile Ala Ala Met Ile Gly Glu Pro Val Met 195 200 Gly Ala Gly Gly Ala Val Pro Pro Pro Asp Tyr Trp Pro Arg Val 215 220 Ala Ala Leu Leu Arg Ser His Gly Ile Leu Leu Ile Leu Asp Glu Val 230 235 Val Thr Ala Phe Gly Arg Thr Gly Thr Trp Phe Ala Ala Glu His Phe 250 245 Gly Val Thr Pro Asp Leu Leu Val Thr Ala Lys Gly Ile Thr Ser Gly 265 260 Tyr Val Pro His Gly Ala Val Leu Leu Thr Glu Glu Val Ala Asp Ala 280 Val Asn Gly Glu Thr Gly Phe Pro Ile Gly Phe Thr Tyr Thr Gly His 295 Pro Thr Ala Cys Ala Val Ala Leu Ala Asn Leu Asp Ile Ile Glu Arg 315 320 305 310 Glu Gly Leu Leu Glu Asn Ala Val Lys Val Gly Asp His Leu Ala Gly Arg Leu Ala Ala Leu Arg Gly Leu Pro Ala Val Gly Asp Val Arg Gln 340 345 Leu Gly Met Met Leu Ala Val Glu Leu Val Ser Asp Lys Thr Ala Arg 360 Thr Pro Leu Pro Gly Gly Thr Leu Gly Val Val Asp Ala Leu Arg Glu 375 Asp Ala Gly Val Ile Val Arg Ala Thr Pro Arg Ser Leu Val Leu Asn 390 395 400 Pro Ala Leu Val Met Asp Arg Ala Thr Ala Asp Glu Val Ala Asp Gly 410 Leu Asp Ser Val Leu Arg Arg Leu Ala Pro Asp Gly Arg Ile Gly Ala 420 425 Ala Pro Arg Arg Gly 435 <210> 4 <211> 818 <212> PRT <213> Streptomyces clavuligerus

Val 1	Tyr	Glu	Cys	Ser 5	Asp	Glu	Val	Arg	His 10	Asp	Val	Pro	Gly	Leu 15	Pro
Gly	Pro	Ser	Pro 20	Ser	Ile	Thr	Val	Leu 25	Gly	Суз	Leu	Gly	Val 30	Arg	Ala
Asp	Gly	Arg 35	Lys	Leu	Glu	Leu	Gly 40	Pro	Pro	Arg	Gln	Arg 45	Ala	Val	Phe
Ala	Leu 50	Leu	Leu	Ile	Asn	Ala 55	Gly	Ser	Val	Val	Pro 60	Val	Asp	Ser	Ile
Val 65	Phe	Arg	Ile	Trp	Gly 70	Asn	Ser	Pro	Pro	Gly 75	Ala	Val	Thr	Ala	Thr 80
Leu	Gln	Ser	Tyr	Val 85	Ser	Arg	Leu	Arg	Lys 90	Leu	Leu	Ala	Glu	Cys 95	Val
Leu	Pro	Asp	Gly 100	Ser	Thr	Pro	Glu	Leu 105	Leu	His	Gln	Pro	Pro 110	Gly	Tyr
Thr	Leu	Ala 115	Leu	Gly	Thr	Glu	His 120	Ile	Asp	Ala	Asn	Arg 125	Phe	Glu	Gln
Ala	Ile 130	Arg	Thr	Gly	Arg	Arg 135	Leu	Ser	Arg	Glu	Glu 140	Gln	His	Gln	Glu
Ala 145	Arg	Ala	Val	Leu	Cys 150	Gln	Ala	Leu	Leu	Ser 155	Trp	Gly	Gly	Thr	Pro 160
Tyr	Glu	Glu	Leu	Ser 165	Ala	Tyr	Asp	Phe	Ala 170	Val	Gln	Glu	Ala	Asn 175	Arg
Leu	Glu	Gln	Leu 180	Arg	Leu	Gly	Ala	Val 185	Glu	Thr	Trp	Ala	His 190	Cys	Суз
Leu	Arg	Leu 195	Gly	Arg	Asp	Glu	Glu 200	Val	Met	Asp	Gln	Leu 205	Lys	Pro	Glu
Val	Gln 210	Arg	Asn	Pro	Leu	Arg 215	Glu	Arg	Leu	Ile	Gly 220	Gln	Leu	Met	Gln
Ala 225	Gln	Tyr	Arg	Leu	Gly 230	Cys	Gln	Ala	Asp	Ala 235	Leu	Arg	Thr	Tyr	Glu 240
Ala	Thr	Arg	Arg	Ala 245	Leu	Ala	Glu	Glu	Leu 250	Gly	Thr	Asp	Pro	Gly 255	Lys
Glu	Leu	Ala	Ala 260	Leu	His	Ala	Ala	Ile 265	Leu	Arg	Gln	Asp	Asn 270	Gly	Leu
Asp	Arg	Val 275	Val	Pro	Ala	Ser	Ala 280	Pro	Pro	Ser	Ala	Gly 285	Val	Gly	Arg
Gly	Ala 290	Val	Thr	Val	Ser	Val 295	Pro	Ala	Gln	Arg	Ser 300	Arg	Pro	Leu	Thr
Arg 305	Pro	Val	Ala	Gly	Arg 310	Ala	Arg	Val	Pro	Gly 315	Ala	Met	Thr	Val	Ala 320
Ala	Gly	Ala	Gly	Ala 325	Ala	Pro	Ala	Ser	Ala 330	Ser	Gly	Ser	Val	Ser 335	Ala
Ser	Val	Ser	Gly 340	Ser	Gly	Ser	Gly	Ser 345	Gly	Ser	Ala	Pro	Ala 350	Ser	Val
Pro	Thr	Phe 355	Phe	Pro	Gly	Ser	Val 360	Ser	Gly	Ser	Ala	Ser 365	Val	Ala	Ala
Ser	Val 370	Ala	Ala	Pro	Val	Ser 375	Gly	His	Val	Ser	Gly 380	Pro	Gly	Ser	Ala
Phe 385	Gly	Ser	Val	Ala	Leu 390	His	Arg	Pro	Gln	Thr 395	Leu	Arg	Gly	Glu	Pro 400
Val	His	Gly	Gly	Ala 405	Gln	Gly	Met	Arg	Thr 410	Gly	Gln	Val	Phe	Pro 415	Thr
Leu	Pro	Pro	Phe 420	Val	Gly	Arg	Gly	Asp 425	Glu	Leu	Arg	Gly	Leu 430	Leu	Glu
Ser	Ala	Thr 435	Ser	Ala	Phe	His	Thr 440	Ser	Gly	Arg	Val	Ala 445	Phe	Val	Val
Gly	Glu	Ala	Gly	Ser	Gly	Lys	Thr	Arg	Leu	Leu	Ser	Glu	Leu	Glu	Arg

455 Ser Val Pro Asp Ser Val Arg Thr Val Trp Ala Ser Cys Ser Glu Ser 470 475 Glu Asp Arg Pro Asp Tyr Trp Pro Trp Thr Thr Val Leu Arg His Leu 490 Tyr Ala Met Trp Pro Glu Arg Met His Gly Phe Pro Gly Trp Leu Arg 505 Arg Ala Leu Ala Glu Leu Pro Glu Val Gly Pro Glu Pro Gln Gly 520 Pro His Ser Pro Asp Gly Glu Glu Asn Ser Gly Asn Gly Asp Gly 535 Ala Gly Asp Gly Asp Ser Thr Pro Ala His Thr Leu Thr Leu Ala Pro 550 555 Ala Leu Ala Pro Pro Arg Ser Arg Glu Ala Arg Phe Thr Leu His Asp 570 Ala Val Cys Gln Ala Leu Leu Arg Thr Val Arg Glu Pro Val Val Ile 585 Met Leu Glu Asp Met Glu Arg Ala Asp Ala Pro Ser Leu Ala Leu Leu 600 Arg Leu Leu Val Glu Gln Leu Arg Thr Val Pro Leu Leu Val Val 615 Thr Thr Arg Thr Phe Arg Leu Ala His Asp Ala Glu Leu Arg Arg Ala 630 635 Ala Ala Val Ile Leu Gln Ser Thr Gly Ala Arg Arg Val Leu Leu Asn 645 650 Ala Leu Asp Ala Arg Ala Thr Gly Glu Leu Ala Gly Gly Met Leu Gly 660 665 Lys Ala Pro Asp Thr Leu Leu Val Arg Ala Leu His Glu Arg Ser Ala 680 Gly Asn Pro Tyr Phe Leu Val Gln Leu Leu Arg Ser Leu Arg Gln Gly 695 Leu Ala Ala Trp Glu Thr Glu Ile Pro Asp Glu Leu Ala Gly Val 715 710 Val Leu Gln Arg Leu Ser Ser Val Pro Pro Ala Val Arg Arg Val Leu 730 Asp Ile Cys Ala Val Val Glu Arg Ser Cys Glu Arg Arg Val Ile Glu 745 Thr Val Leu Arg His Glu Gly Ile Pro Leu Glu Asn Val Arg Thr Ala 760 Val Arg Gly Gly Leu Leu Glu Glu Asp Pro Asp Pro Gly Arg Leu 775 Arg Phe Val His Pro Leu Val Arg Glu Ala Val Trp Asp Asp Leu Glu 790 795 Asn Thr Arg Arg Pro Val Ser Arg Ser Ser Ala Leu Gly Ala Leu Ala 805 810 815 Thr Val

<210> 5

<211> 1330

<212> DNA

<213> Streptomyces clavuligerus

<400> 5

gtgcccggct ccggactcga agcactggac cgtgccaccc tcatccaccc caccctctcc ggaaacaccg cggaacggat cgtgctgacc tcggggtccg gcagccgggt ccgcgacacc gacggccggg agtacctgga cgcgagcgcc gtcctcgggg tgacccaggt gggccacggc

cgggcc	gagc	tggcccgggt	cgcggccgag	cagatggccc	ggctggagta	cttccacacc	240
tggggg	gacga	tcagcaacga	ccgggcggtg	gagctggcgg	cacggctggt	ggggctgagc	300
ccggag	ıccgc	tgacccgcgt	ctacttcacc	agcggcgggg	ccgagggcaa	cgagatcgcc	360
ctgcgg	gatgg	cccggctcta	ccaccaccgg	cgcggggagt	ccgcccgtac	ctggatactc	420
tcccgc	cggt	cggcctacca	cggcgtcgga	tacggcagcg	gcggcgtcac	cggcttcccc	480
gcctac	cacc	agggcttcgg	cccctccctc	ccggacgtcg	acttcctgac	cccgccgcag	540
ccctac	cgcc	gggagctgtt	cgccggttcc	gacgtcaccg	acttctgcct	cgccgaactg	600
cgcgag	jacca	tcgaccggat	cggcccggag	cggatcgcgg	cgatgatcgg	cgagccgatc	660
atgggc	gcgg	tcggcgccgc	ggccccgccc	gccgactact	ggccccgggt	cgccgagctg	720
ctgcac	tcct	acggcatcct	gctgatctcc	gacgaggtga	tcacggggta	cgggcgcacc	780
gggcac	tggt	tcgccgccga	ccacttcggc	gtggtcccgg	acatcatggt	caccgccaag	840
ggcatt	cacc	tcggggtatg	tgccgcacgg	cgccgtcctg	accaccgagg	ccgtcgccga	900
cgaggt	cgtc	ggcgaccagg	gcttcccggc	gggcttcacc	tacagcggcc	atgccacggc	960
ctgcgc	ggtg	gccctggcca	acctggacat	catcgagcgc	gagaatctgc	tcgacaacgc	1020
cagcac	cgtc	ggcgcctacc	tgggcaaacg	cctggccgag	ctgagcgatc	tgccgatcgt	1080
cgggga	cgtc	cggcagaccg	gtctgatgct	cggtgtcgaa	ctggtcgccg	accgcggaac	1140
ccggga	igccg	ctgccgggcg	ccgccgtcgc	cgaggccctg	cgcgagcggg	cgggcatcct	1200
gctgcg	lcdcc	aacggcaacg	ccctcatcgt	caaccccccg	ctgatcttca	cccaggaaga	1260
cgccga	cgaa	ctcgtggcgg	gcctgcgctc	cgtactcgcc	cgcaccaggc	cggacggccg	1320
ggtgct	ctga						1330

<210> 6

<211> 3345

<212> DNA

<213> Streptomyces clavuligerus

<400> 6

atgaagtacg acataaccc accatcegge etteggtteg aceteetegg eeggtgace 60 gtgacegeg gegageace egtggacetg ggeggegeac ggeagegeg eetgetegee 120 etgetgetea tegatgtegg eaacgtggte eeggtgeegg teatgacege gtegatetgg 180 ggggeegace eacegteeeg ggteegggg acgeteeagg ettatgtgte eegactgegg 240 aaacteetge acegeeatga eegtteeett egeettgtee aceageteea ggggtatete 300 etegaagtgg atteggegaa gg